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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,994	03/03/2004	Alberto Orfao De Matos Correia E Valle	DE MATOS CORREIA E VALLE	4880

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
10/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/791,994	DE MATOS CORREIA E VALLE ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/8/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response, filed August 6, 2007, is acknowledged and has been entered. The specification has been amended. Claims 1, 13, 16, 18, 19, 22, 31, 32, and 34 have been amended. Claims 23, 24, and 35 have been deleted. Accordingly, claims 1-22 and 25-34 are pending and remain under examination.

Withdrawn Rejections or Objections

2. All rejections or objections not reiterated herein, have been withdrawn.

3. The rejections of claims 23, 24, and 35 are now moot, in light of Applicant's cancellation of the claims.

4. In light of Applicant's amendment and arguments, the rejection of claims 1, 3, 6-13, 15-17, 19, 20, 25, and 34 under 35 U.S.C. 103(a) as being unpatentable over Nagler et al. (Detection of Minimal residual disease (MRD) after bone marrow transplantation (BMT) by multi-parameter flow cytometry (MPFC), Medical Oncology 16: 177-187 (1999)), is hereby, withdrawn.

5. In light of Applicant's amendment and arguments, the rejection of claims 2, 4, 5, 18, 21, 22, 26, 27, and 30-33 under 35 U.S.C. 103(a) as being unpatentable over Nagler et al. (Detection of Minimal residual disease (MRD) after bone marrow

transplantation (BMT) by multi-parameter flow cytometry (MPFC), Medical Oncology 16: 177-187 (1999)) in view of Ward et al. (US Patent 5,627,037) is hereby, withdrawn.

6. In light of Applicant's amendment and arguments, the rejection of claims 2, 14 and 26-33 under 35 U.S.C. 103(a) as being unpatentable over Nagler et al. (Detection of Minimal residual disease (MRD) after bone marrow transplantation (BMT) by multi-parameter flow cytometry (MPFC), Medical Oncology 16: 177-187 (1999)) in view of Orfao De Matos et al. (US Patent 6,913,901), is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-22 and 25-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in being incomplete because step g) fails to clearly define a requirement set forth in the preamble. Specifically, the preamble recites, "A method for identification of aberrant phenotype expressed by neoplastic cells;" however, step g) only cites "establishing the phenotypic aberrations ... that allow their identification and distinction...". Perhaps, Applicant intends, "establishing and identifying the phenotypic aberrations ... that provide their identification and distinction...".

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-22 and 25-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for using monoclonal antibody combinations having in common at least three fluorochrome-conjugated antibodies specific for tumor cells of interest contained in the neoplastic samples that vary in type, lineage, and maturation stage, and obtaining at least two light scatter measurements and at least four fluorescence intensity measurements of each stained cell in each of the samples, does not reasonably provide enablement for using monoclonal antibody combinations having in common any at least three fluorochrome-conjugated antibodies with undefined specificities, and obtaining only fluorescence emissions measurements of each stained cell in each of the normal/reactive and neoplastic samples. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include 1) the nature of the

invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

While the specification provides guidance and working example in the specification wherein the at least three common fluorochrome-conjugated antibodies are specific for tumor cells of interest contained in the neoplastic samples that vary in type, lineage, and maturation (page 11, line 8 to page 12, line 3 and Example 3), the specification does not show any working examples of the claimed method using any common combination of at least three monoclonal antibodies that are specific for any normal or non-specific abnormal cells. The fact that the claimed method appears to work using in common tumor-specific at least three fluorochrome-conjugated monoclonal antibodies, is not sufficient to enable the breadth of the claimed method for any and all possible at least three monoclonal antibodies in common. The specification does not establish a direct correlation between tumor-specific monoclonal antibodies and any three monoclonal antibodies, which would lead the skilled artisan to say that if the claimed method works when they are tumor-specific, then it should also work for any combination of three monoclonal antibodies in common specific for any cell surface antigens that are expressed by any cells including those exclusively expressed by normal/reactive cells, to enable the breadth of the claimed method. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the

breadth of the claimed method is enabled. This is not the case in the instant specification.

With respect to the measurements obtained from each stained cell and microbead in the samples, the claimed method recites sequential measurement of only fluorescence emissions associated to large numbers of cells stained with each of the combinations of monoclonal antibodies from the normal/reactive samples and neoplastic sample, without any limitation as to the number of fluorescence emissions measurements are performed for each cell. Page 13, second full paragraph of the specification; however, provides that for each stained cell in the samples and microparticle, at least two measures of light scatter and at least four measures of fluorescence emissions should be taken, sequentially measured per sample aliquot, stored into two independent list mode data files, merged into a new data file whereupon phenotypic aberrations are established, identified, and defined, in order for the method to work. In page 18, first full paragraph of the specification, it is stated that it is by quantifying the amount of measurements of light scatters and fluorescence emissions for each individual population of neoplastic cells as compared to those populations of normal cells stained with identical panels, that statistical information on the most discriminant aberrant phenotypes displayed by the neoplastic cells can be derived. Each aberrant phenotype may be composed of a combination of two or more light scatter and fluorescence measurements. The breadth of the claims encompass only using measurement of fluorescence emissions by stained cells; without specifically stating how phenotypic aberrations can be established and defined without undue

experimentation, absent specific recitation of required at least two light scatter measurements and at least four fluorescence intensity measurements, which is commensurate in scope with Applicant's disclosure.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

9. Applicant's arguments with respect to claims 1-22 and 25-34 have been considered but are moot in view of the new ground(s) of rejection.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 8:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gailene R. Gabel
Primary Examiner
Art Unit 1641

October 26, 2007